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On the Front Line of Improving Treatment for Wounded Warriors

Filed under HEATH, MENTAL HEALTH, RESEARCH AND DEVELOPMENT

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By Dr. Madelaine Paredes, research scientist, NAMRU-SA, Combat Casualty Care and Operational Medicine



Navy Medicine is a global healthcare network of 63,000 Navy medical personnel around the world who provide high quality health care to more than one million eligible beneficiaries. Navy Medicine personnel deploy with Sailors and Marines worldwide, providing critical mission support aboard ship, in the air, under the sea and on the battlefield.

I was determined to pursue a career in science, so I decided to join the Cellular and Structural Biology $\label{eq:UTHSCSA} \text{UTHSCSA}.$

Editors note: Dr. Madelaine Paredes wants to inspire future women and minority scientists to pursue their goals. Her perseverance in research will contribute to continuing improvements in the quality of treatment of our wounded warriors. Follow her dedicated journey from her native Colombia to

When I started college as a microbiology student in my native country of Colombia, I never imagined where my career would take me through the years.

The desire to learn and discover biology had started earlier in my childhood years looking at microbes and plant cells under a Navy Medicine Social Media

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research at NAMRU-SA.



The desire to learn and discover biology had started earlier in my childhood years looking at microbes and plant cells under a microscope in my biology classes.

microscope in my biology classes. It was then as a young scientist that I developed a profound passion for research and the joy of understanding many biological processes in great detail. Therefore, in the last semester of college I applied to be part of a research team outside of Colombia where I would apply the knowledge I acquired through college and learn from the experience of established research scientists. I was thrilled to be accepted as a

research fellow in the laboratory of two renowned scientists in the field of Calcium (Ca2+) signaling, Drs. Patricia Camacho and James D. Lechleiter in the department of Physiology at the University of Texas Health Science Center at San Antonio (UTHSCSA).

This was such a great experience because I was being exposed for the first time to advanced technology in the field of cellular imaging and molecular biology used as tools to understand cellular signaling. Additionally, I was able to interact with other students and post-docs from different cultural and scientific backgrounds which broadened my view of the research environment. From this exposure I was determined to pursue a career in science, so I decided to join the Cellular and Structural Biology graduate program at UTHSCSA.

As part of my doctoral dissertation, I performed research on the relationship between protein processing in the endoplasmic reticulum (ER) and Ca2+ signaling. The ER is the major intracellular Ca2+ storage center and it is also the organelle where proteins that travel through the secretory pathway are synthesized and processed. Moreover, it has been shown that disrupting these two functions of the ER, Ca2+ storage and protein processing, causes ER stress and



My research will help healthcare providers and caregivers in tailoring treatment for individuals affected with schizophrenia.

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induces the Unfolded Protein Response (UPR). Under the UPR, if the cell cannot recover its normal functions, it will activate cell death pathways. During my graduate studies, I developed imaging assays to monitor the impact of ER Ca2+ depletion on protein processing and the effect that protein misfolding may have on ER Ca2+. These studies revealed the importance of maintaining anappropriate ER homeostasiswhere alterations in Ca2+ homeostasis are sufficient to affect processing of proteins and induce cell death. These findings were published in the journal *Cell Calcium*, where I was first author. As part of my research on Ca2+ signaling and in collaboration with members from Dr. James Lechleiter's lab, I also studied the role that Calcineurin (CN), a Ca2+ dependent phosphatase, has on the UPR. We found that CN gets activated by an increase in cytosolic Ca2+ due to Ca2+ leakage from the ER and binds to the ER protein kinase PERK. The association between CN and PERK enhances protein synthesis inhibition, and CN indirectly aids in restoring ER Ca2+ homeostasis. These findings were published in *Plos One*, where I shared first authorship.

For my first post-doctoral appointment, I joined the Department of Psychiatry at UTHSCSA under the supervision of Dr. Consuelo Walss-Bass. I worked on different projects trying to understand the molecular causes of psychiatric disorders such as schizophrenia, bipolar disorder, and depression as well as trying to find biomarkers for those diseases. I developed a profound desire to understand the contribution of signaling from the immune system in psychiatric diseases and how the brain could be modulated by those signals in such a way that could lead to pathological outcomes. From my interaction and collaborations with experts in the field of Psychiatry, it became clear to me that those devastating disorders are multifactorial. Moreover, there is a great need to understand the molecular underpinnings of how the brain works and controls our behavior to design better therapeutic strategies.



I will continue performing research to improve physicians' diagnosis and clinical decision making with respect to trauma-injured patients and hopefully improve the quality of treatment of our wounded warriors.

Some of my research in that field involved understanding the molecular side effects of medications psychiatric disorders such schizophrenia. Here we found that even though these medications are great in treating some of the symptoms of the disease, they also can cause metabolic disturbances that need to be carefully monitored on each individual to avoid secondary complications such as diabetes and cardiovascular diseases. My research will help healthcare providers and caregivers in tailoring treatment for individuals affected with schizophrenia. Those findings have been published recently in the International Journal of Neuropsychopharmacology, as well as Plos One and Schizophrenia Research. As part of my work as a post-doc in the

Department of Psychiatry, I have two other publications that are under preparation.

For my second post-doctoral position, I joined the Naval Medical Research Unit San Antonio (NAMRU-SA) research team early this year as an Oak Ridge Institute for Science and Education (ORISE) post-doctoral Fellow. I started my work with Dr. Rene Alvarez and CDR Forest Sheppard as my mentors where, together with a great team of scientists, I have been studying the contribution of the immune response in traumatic-hemorrhage in animal models. My previous experience as well as my perseverance in research let me to be invited to join NAMRU-SA as a research scientist sponsored by the Henry M. Jackson Foundation. I will continue performing research to improve physicians' diagnosis and clinical decision

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making with respect to trauma-injured patients and hopefully improve the quality of treatment of our wounded warriors.

One of my goals is to become an independent scientist, establishing collaborations with other researchers and promoting scientific education. I belong to a minority Hispanic group, and I understand the importance of encouraging underrepresented groups to be part of scientific research. Moreover, I would like to inspire future minority scientists in pursuing their goals.

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